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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Su Chen

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EXAMINER

WEISZ, DAVID G

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

04/13/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/696,051	Applicant(s) CHEN, SU	
	Examiner DAVID WEISZ	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/15/09.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-17 and 30-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-17 and 30-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Acknowledgement is made of the amendment filed 12/15/09. Upon entering the amendment, the claims 1, 9, 30 and 37 are amended. Claims 1-4, 6-17 and 30-56 are pending and presented for the examination.

Claim Objections

2. Applicant is advised that should claim 1, 9, 30 or 37 be found allowable, claim 2, 14, 33 or 42, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-4, 6-17 and 30-56 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 1, 9, 30 and 37, the claims disclose the addition of an unlabeled organic acid and measuring a unlabeled and labeled organic acid. Does the sample contain unlabeled *and* labeled organic acids? If so, which labeled organic acid is the focus of measurement? The specification, in paragraph [0007], discloses that a labeled internal standard is used to make adjustments to an unlabeled sample, to correct for loss during processing. The claims will be interpreted in that the sample contains only unlabeled organic acids and the internal standard is a similar or identical labeled organic acid. Thus it appears that the instant claims recite conventional usage of a labeled internal standard for quantifying an analyte of a similar nature by mass spectrometry.

5. Claims 7-8, 12-13, 31-32 and 40-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to a processing step, discussing enrichment and chemical modification. What does enrichment of the unlabeled organic acid actually entail? What sort of chemical modifications are taking place? These steps, as they are currently disclosed, are unclear and indefinite.

Claim Rejections - 35 USC § 103

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. **Claims 1-4 and 7-16** are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson et al. (*Journal of Lipid Research*, 1988) (Peterson) in view of Nguyen et al. (US 2005/0070023) (Nguyen).

Regarding claims 1-4, Peterson discloses a method of labeling glycolic acid with an oxygen-18 atom at the carboxyl group (page 95, Col2). Further the reference discloses a method of sample analysis using gas and liquid chromatography mass spectroscopy (page 95, Col2).

However, the reference does not specifically disclose the oxygen-18 labeled acid for use as an internal standard, nor the processing step of the sample.

Nguyen discloses a method of using stable isotope labeled internal standards in analysis of carboxylic acids (abstract). Using internal standards to quantify analytes samples in analysis is a well known practice in analytical chemistry, and Nguyen discloses that using oxygen-18 isotopes as internal standards in mass spectrometry is used for quantification of an analyte [0004]. Nguyen additionally discloses that the entire sample is processed via a chemical modification to convert the sample into a carboxylic acid ester prior to mass spectrometry [0025]. One having ordinary skill in the art would use the internal standard technique of Nguyen and the labeled glycolic acid of Peterson in a GC-MS or LC-MS analysis as it would allow one to quantify an unlabeled glycolic acid analyte by measuring structurally similar labeled internal standards.

Further, one having ordinary skill in the art would be able to adjust an amount of unlabeled analyte, as is well known in the use of internal standards, using the method of Nguyen combined with Peterson.

Regarding claims 7-8, Peterson-Nguyen disclose all of the limitations as addressed above regarding the processing of the sample.

Regarding claim 9, Peterson-Nguyen disclose all of the limitations as addressed in claim 1 above. Further, the application of the above method to the other disclosed organic acids would have been obvious, as according to applicant's disclosure, they are patentably indistinct.

Regarding claim 10-11, the references disclose all of the limitations as addressed above. Further, it would have been obvious to apply the method to a sample containing more than one organic acid, as it would require only routine skill in the art to differentiate several species using mass spectroscopy.

Regarding claims 12-16, the references disclose all of the limitations as addressed above regarding processing and the specific type of mass spectrometry.

8. **Claims 6, 17 and 30-56** are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson in view of Nguyen, as applied to claims 1-4 and 7-16 above, further in view of Pang (*HKMJ*, 1996) (Pang).

Regarding claims 6 and 17, Peterson-Nguyen disclose all of claim limitations as applied to claim 1, above. However, the references do not specifically disclose that the method extends to analyzing urine.

Pang discloses a method of analyzing urine, and that accumulation of organic acids in urine is associated with many metabolic disorders (Page 269, "Organic Acid Analysis"). As the method of Peterson-Nguyen accurately determines the levels of carboxylic acids via GC-MS and LC-MS using oxygen-18 internal standards, one having ordinary skill in the art would naturally use the method in conjunction with the method of Pang, as it would increase accuracy of analysis.

Regarding claim 30, 36-37 and 45, Peterson-Nguyen-Pang disclose all of the claim limitations as referenced above. With this in mind, it would only require routine

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skill in the art to determine the accumulation of organic acids, as described by Pang, to diagnose the metabolic defect.

Regarding claims 31-35 and 40-44, Peterson-Nguyen-Pang disclose the processing and specific type of mass spectrometry already described above.

Regarding claims 38-39 and 54-56, Peterson-Nguyen-Pang already disclose that it would have been obvious to apply the method to a sample containing more than one organic acid.

Regarding claims 46-53, Peterson-Nguyen-Pang already disclose that application of the above method to the other disclosed organic acids would have been obvious, as according to applicant's disclosure, they are patentably indistinct.

Response to Arguments

9. Applicant's arguments with respect to claims 1-4, 6-17 and 30-56 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID WEISZ whose telephone number is (571)270-7073. The examiner can normally be reached on Monday - Thursday, 7:30 a.m. - 5:00 p.m., EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

4/11/2010

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

/D. W./
Examiner, Art Unit 1797